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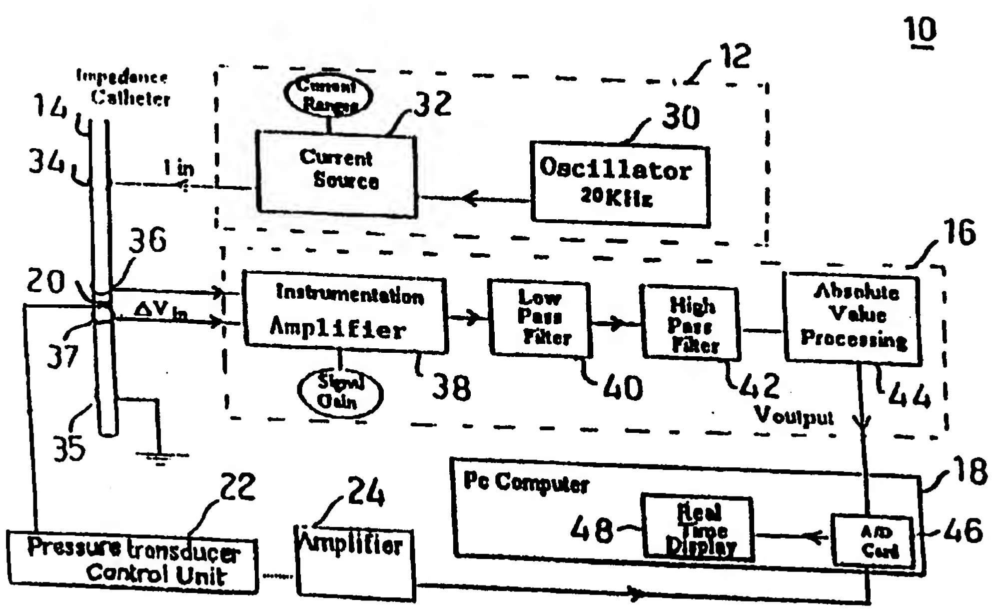

(57) Abstract

Impedance catheter (14) has two outer electrodes (34, 35), and two central electrodes (36, 37). A signal processor (16) comprises an instrumentation amplifier (38) connected between voltage electrodes (36, 37), to sense the voltage developed thereon by the output current of current source (32). A DC output voltage is determined based on the potential difference of voltage electrodes (36, 37), which is converted into an impedance value. The cross-sectional area A is derived from the impedance value.

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BLOOD VESSEL CROSS-SECTIONAL AREA DETECTOR AND COMPLIANCE MEASUREMENT DEVICE AND METHOD

FIELD OF THE INVENTION

The present invention relates generally to medical diagnostic instrumentation equipment, and more particularly, to an on-line system for examining coronary and vascular cross-sectional areas to detect blockage of arteries and estimate coronary compliance using an electronic impedance method.

BACKGROUND OF THE INVENTION

Heart disease and coronary/vascular disorders are among the largest contributors to the total number of medical fatalities recorded by medical surveys of the adult population. The greatest cause of coronary/vascular disorders stems from the onset of arterosclerosis, which if undetected, almost certainly leads to stroke, or varying degrees of heart attack, with the resultant consequences of permanent disability and in many cases, premature death.

Existing diagnostic techniques for detecting arteriosclerosis and cardiac stenosis include those associated generally with angiocardiography. Specific diagnostic techniques include methods for detecting blood flow and volume changes such as that discosed in US Patent 5,343,867 to Shankar. This patent discloses a method for detecting the onset of arteriosclerosis by use of apparatus

for sensing an arterial blood volume differential while varying the induced pressure applied via a pressure cuff. The apparatus uses an electrical impedance plethysmograph and a volume plethysmograph and presents data relating to the patient's arterial peak compliance.

In US Patent 5,423,323 to Orth, there is disclosed a system for calculating compliance and cardiac hemodynamic parameters of blood vessels, using a catheter having a displacement balloon and pressure transducer in connection with a blood flow monitor and calibration system. A processor determines the change in blood pressure caused by the volume displacement of the balloon.

In US Patent 4,840,182 to Carlson, a conductance catheter apparatus is disclosed for measuring the volume of a biological chamber. The catheter is constructed with a plurality of electrodes along its length, including outer and inner electrodes, arranged such that AC signals at high and low frequencies applied to the outer electrodes induce conductance signals in the inner electrodes via the chamber wall. The inner electrodes are connected to processing circuitry for determining volume in manner that excludes parallel conductance via tissue.

During the performance of angioplasty techniques to detect cardiac stenosis, it would be useful to have on-line data on the coronary compliance to help in selecting the preferred medical approach to be applied in removing the stenosis. Existing diagnostic techniques are not suited to provide such measurements on-line.

Therefore, it would be desirable to provide a method for measuring arterial compliance on-line during catheterization, to detect cardiac stenosis and to assess the result after angioplasty, for determining the proper therapeutic treatment.

SUMMARY OF THE INVENTION

Accordingly, it is a principal object of the present invention to overcome the problems associated with prior art coronary diagnostic techniques and provide a method and apparatus for on-line measurement of the dynamics of arterial dimensions during cardiac catheterization by use of electrical impedance measurements. These measurements are used to provide information about the cross-sectional area of the arteries at any point, and can be used to calculate vessel wall compliance, and the location of blockages or potential areas of blockage.

In accordance with a preferred embodiment of the present invention, there is provided a blood vessel cross-sectional area detector comprising:

a catheter having at least a first pair of electrodes spaced apart from one another, and a second pair of electrodes spaced apart from one another;

means for measuring a voltage developed between said second pair of electrodes when a current is passed through said first pair of electrodes while inserted into a blood vessel;

means for converting said measured voltage into an

impedance value representing a cross-sectional area of said blood vessel, and calculating said cross-sectional area;

means for measuring blood pressure in said blood vessel;

means for calculating a compliance value of said blood vessel based on said cross-sectional area and blood pressure; and

means for displaying said calculated blood vessel compliance value.

In a preferred embodiment, a specially designed catheter is constructed having a pressure sensor and electrodes for measuring electrical impedance. The first pair of catheter electrodes is connected to a current source, and the second pair is connected to an instrumentation amplifier for sensing the voltage developed by current flow through the first set of electrodes. When the catheter is inserted into the arteries, impedance measurements are made along the length of the artery, providing information about the cross-sectional area at any given point. This information, together with arterial blood pressure, which is measured at the same location and point in time, is used to calculate blood vessel wall compliance, which can be displayed.

The vessel wall compliance measurement is a very significant factor in determining whether or not hardening of the arteries is present, and if so, at what points, which ultimately assists in the determination of the best

therapeutic treatment for clearing blockages in the arteries or potential areas of blockage. Possible therapeutic treatments to be considered include angioplasty, drilling or other techniques that are useful in clearing blockages. Selection of the devices for treatment can be based on the information derived from the compliance value.

A feature of the invention is the application of the impedance method to coronary arteries rather than the ventricle.

Other features and advantages of the invention will become apparent from the following drawings and description.

BRIEF DESCRIPTION OF THE DRAWINGS

For a better understanding of the invention with regard to the embodiments thereof, reference is made to the accompanying drawings, in which like numerals designate corresponding elements or sections throughout, and in which:

Fig. 1 is a schematic block diagram of a preferred embodiment of a blood vessel cross-sectional area detector and compliance measurement device, constructed and operated in accordance with the principles of the present invention;

Fig. 2 is an electronic block diagram of the system of Fig. 1, showing an impedance catheter and instrumentation;

Fig. 3 is a detailed view of the catheter construction;

Fig. 4 is a flowchart showing an application of the inventive method for measuring and displaying a compliance value;

Figs. 5a-b illustrate typical signal waveforms for an ECG and blood pressure measurements of a dog specimen:

Fig. 5c illustrates typical signal waveforms for blood vessel dimension measurements, using a known ultrasound method;

Fig. 5d illustrates typical signal waveforms for blood vessel dimension measurements, using the inventive method;

Figs. 6a-b show layout configurations for performing a stenosis search in a latex tube simulating a blood vessel;

Figs. 7a-c and Fig. 8 illustrate diameter measurements using the inventive method in the stenosis search of Figs. 6a-b;

Figs. 9a-c illustrate diameter measurements using the inventive method in a stenosis search in a dog specimen; and (Fig.10) Table 1 illustrates actual and measured narrowing of blood vessel diameters derived using the inventive method.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to Fig. 1, there is shown a schematic block diagram of a preferred embodiment of a blood vessel cross-sectional area detector and compliance measurement device 10, constructed and operated in accordance with the principles of the present invention. Device 10 comprises a signal source 12, an impedance catheter 14, a signal processor 16, and a display and analysis system 18. Blood pressure information is provided by a microtip catheter pressure transducer 20, a transducer control unit 22, and an amplifier 24.

In general, when the catheter is inserted into the arteries, impedance measurements are made along the length of the artery, providing information about the cross-sectional area at any given point. This information, together with arterial blood pressure, which is measured at the same location and point in time, is used to calculate vessel wall compliance, which can be displayed.

Signal source 12 is typically provided as a source of electrical current, which is fed through electrodes on impedance catheter 14, to develop a voltage thereon. The voltage measurement is sensed and amplified by signal processor 16, typically a Fast Settling, FET input, very high accuracy instrumentation amplifier. This information is filtered and ultimately provides a resistance measurement which can be converted to a real-time display on a PC computer, such as is represented by display and analysis system 18.

Referring now to Fig. 2, there is shown an electronic block diagram of the system of Fig. 1, showing impedance catheter 14 and instrumentation. Signal source 12 comprises an oscillator 30 providing a bipolar square wave output without a DC component, at a frequency of 20 kHz. The amplitude of the current output can be varied by current source 32 between 25-250 microamps. Impedance catheter 14 has a plurality of electrodes mounted thereon in spaced apart fashion, two outer electrodes (current) 34, 35 and two central electrodes (voltage) 36, 37. As shown in the block diagram, current source 32 is connected so as to inject the signal between outer current electrodes 34, 35, with the latter being grounded.

Signal processor 16 comprises an instrumentation amplifier 38 as described previously, connected between voltage electrodes 36, 37, to sense the voltage developed thereon by the output current of current source 32. After amplification of the differential voltage /¥ Vin measured

between voltage electrodes 36, 37, the signal is filtered in low pass, high pass filters 40, 42. It is then passed to absolute value detector 44, to determine a DC output voltage which is proportional to the potential difference measured between the voltage electrodes 36, 37.

The output of detector 44 is then sampled at a sampling rate of 200 Hz, and fed to A/D converter 46, which is resident in a PC computer forming the basis for display and analysis system 18. The digital voltage value is then converted into an impedance value and displayed on display monitor 48. The cross-sectional area A is then extracted from the impedance value via a well-known conversion which can be expressed as:

$$A = \frac{p * L}{R} \qquad (1)$$

where R is the measured resistance, p is the specific resistivity, and L is the distance between voltage electrodes.

Impedance catheter 14 is constructed with a pressure transducer 20 disposed therein, which is connected to a pressure transducer control unit 22. The signal supplied by transducer 20 is amplified by amplifier 24, and fed to A/D converter 46 in display and analysis system 18. By combining the impedance catheter 14 measurements providing the dynamic cross-sectional area of a blood vessel at any point, with the blood pressure information at the same point from pressure transducer 20, the vessel wall

compliance can be calculated at the selected point.

Referring now to Fig. 3, there is shown a detailed view of the construction of impedance catheter 14, comprising four electrodes. The catheter 14 comprises a polyethylene sleeve 54, in which a stiffening wire 56 is disposed. A heat-shrink tube 58 encompasses sleeve 54, and between sections thereof there are placed ring-shaped outer electrodes 34, 35, and central electrodes 36, 37, which are exposed. The spacing between outer electrodes 34-35 is defined as d, and the spacing between central electrodes 36-37 is defined as L. The pressure transducer 20, which is of the type normally used with catheters, is embedded in polyethylene sleeve 54, and is exposed via an opening 55 therein.

Referring now to Fig. 4, there is shown a flowchart of the steps outlining the procedure employed in the inventive method. Initially, in block 60, impedance catheter 14 is placed in the artery which is chosen for measurement of the vessel wall compliance. In block 62, the current and gain of instrumentation amplifier 38 are set. In block 64, a voltage measurement is taken as catheter 14 is pulled back along the artery, thereby enabling measurements along the entire length of the artery. This step can be repeated as often as needed to obtain different measurements from different sites along the vessel walls, or to obtain measurements from different vessels entirely. In block 66, the voltage measurements are converted into the measured

resistance.

In block 68, measurement of the blood specific conductivity is made, and this information is utilized in block 70, in which the impedance measurement is converted into an arterial cross-sectional area, according to the mathematical relationship defined in equation (1) above. In block 70, the blood vessel diameter is extracted. In block 74, blood pressure measurement information is obtained from pressure transducer 20.

When the dynamic cross-sectional area data from block 70 is combined with the arterial blood pressure from block 74, taken at a specific location along the artery, a compliance calculation is made in accordance with known techniques in block 76 and the value is displayed in block 78 for diagnostic purposes.

A major feature of the present invention is the application of the impedance measurement method to coronary arteries rather than the ventricle. Another new feature is the use of a specially designed catheter which allows a measurement of both the pressure and electrical impedance, enabling calculations to determine both the potentially blocked regions of the artery and the compliance of the segments. The actual location of the potentially blocked or stenosed area is determined by a combination of X-ray scanning, to provide the location of the catheter as it travels through the artery, and the obtained measurements.

In Figs. 5a-d, there are shown the results of experiments conducted on the vascular system of a dog

specimen, and these are shown as signal waveforms representing the ECG (Fig. 5a) signal, the blood pressure (Fig. 5b), the blood vessel diameter measured using an ultrasound technique (Fig. 5c), and the blood vessel diameter measured using the inventive impedance technique (Fig. 5d), obtained in the descending aorta of the dog. The catheter used in these experiments was constructed with the electrodes spaced apart with dimensions d=3 cm and L=0.52 cm.

It is important to note that the blood vessel diameter as measured by ultrasound in Fig. 5c follows a similar wave pattern of arterial pressure as in Fig. 5b. Note that the blood vessel diameter as measured by the impedance method in Fig. 5d is very similar to the Fig. 5c ultrasound diameter measurement.

In Figs. 6a-b, experimental search configurations are shown for performing a stenosis search in a simulated environment. A latex tube 80 having an outside diameter of 9 mm, and an interior diameter of 6 mm, is provided to simulate a blood vessel. As shown in Fig. 6a, a latex ring 82 is provided having an interior diameter of 9 mm, an outer diameter of 18 mm, and a width of 0.5 cm. Ring 82 is placed over tube 80, but practically does not constrict it, so that the simulated blood vessel does not contain a stenosis. In Fig. 6b, however, a stenosis is present, as simulated by ring 82 placed over another latex tube 84, which has an outside diameter of 11 mm, and an interior diameter of 7.5 mm, without the stenosis. At the location of the stenosis,

the interior diameter narrows to 6.7 mm.

After insertion of the catheter 14 into tube 80, an artificial blood flow was created using a liquid circulating through a pulsitile pump, operated at 65 beats per second. The search was conducted by pulling back catheter 14, and measuring the diameter and the distance from the origin of the search, via the A/D converter 46 shown in the Fig. 1 electronic block diagram. The search was performed using three catheter configurations, in which the spacing between the voltage electrodes 36, 37 was varied: 1) d = 5 cm, L = 0.24 cm 2) d = 5 cm, L = 0.48 cm and 3) d = 5 cm, L = 0.96 cm. A conductivity meter was used to measure the specific conductivity of the liquid used, and the search was carried out in each of the two latex tubes of Figs. 6a-b.

In Figs. 7a-c and Fig. 8, there are illustrated diameter measurements obtained using the inventive method in the stenosis search of Figs. 6a-b. The waveforms of Figs. 7a-c correspond to the latex tube 80 shown in Fig. 6a, and the waveform of Fig. 8 corresponds to latex tube 84 shown in Fig. 6b.

Each of Figs. 7a-c corresponds to one of the three catheter configurations described above. In Figs. 7a-c, the tube diameter is shown as a function of the catheter 14 location relative to the origin point, and the waveforms show the location of the stenosis, at which the blood vessel wall is thickened, exactly at the .25 mm point from the origin. At this point, the amplitude of the change in diameter over a portion of tube length is the smallest, over

the entire tube length searched. In each of the waveforms of Figs. 7a-c, a slight drop in the baseline value of the diameter is shown, in the area of the stenosis, and this is due to the fact that latex ring 82 applies some pressure to the latex tube 80 even when there is no pulsitile flow.

The length of the stenosis measured by the different catheters 14 is influenced by the individual catheter configurations. Although it is difficult to precisely define the boundaries of the stenosis, it appears that as the spacing between the voltage electrodes 36, 37 increases, the length of the stenosis increases.

In the waveform of Fig. 8, based on the experimental search configuration of Fig. 6b, the location of the stenosis can be clearly seen during pulsitile flow, as a function of time. As with the search configuration of Fig. 6a, there is shown a decrease in the amplitude of the change in diameter over a portion of the tube 84 length. However, in contrast with the search configuration of Fig. 6a, there is a significant decrease in the baseline diameter, i.e, in the measured diameter at the minimum diameter point, as a result of narrowing of the localized diameter value.

In Figs. 9a-c, there are shown typical signal waveforms for blood vessel diameter measurements, using the inventive method during the attempt to locate a stenosis in the aortic vessel. The catheter 14 was placed a few centimeters proximate the stenosis, and the diameter was

recorded according to the impedance method, while pulling back catheter 14. Three experiments were conducted in the descending aorta of the dog, to search for the localized stenosis. In each experiment, a different degree of narrowing was applied artificially. The results are shown in Figs. 6a-c, and as before, the catheter used in these experiments was constructed with d=3 cm and L=0.52 cm.

In Table 1, (Fig.10) a summary of the measurement results of the three experiments is shown, with the magnitude of the stenosis calculated by measurement of the perimeter of the blood vessel before and after the location of the stenosis. From the perimeter measurement the diameter was extracted, and the magnitude of the actual stenosis was obtained as the difference in the diameters. The measured stenosis was calculated as the difference between the measured diameter at the beginning of the search point, and the minimum diameter measured at the center of the stenosis.

As can be seen, it is possible to locate, by impedance measurement, the location of the stenosis in the aortic vessel even when the degree of stenosis is the least, only 18% or less, which represents the diameter narrowing as a percentage of the actual aorta diameter (16.45 mm). With an increase in the magnitude of the stenosis, there was a similar increase in the measured stenosis using the impedance method. However, as expected, the magnitude of the stenosis measured by the impedance method was consistently smaller than the actual stenosis.

In summary, the method of the present invention

enables measurement of blood vessel wall compliance, which is a very significant factor in determining whether or not hardening of the arteries is present. Location of the stenosis and knowledge of its characteristics ultimately assist in the determination of the best therapeutic treatment for clearing blockages in the arteries or potential areas of blockage.

Having described the invention with regard to certain specific embodiments thereof, it is to be understood that the description is not meant as a limitation, since further modifications may now suggest themselves to those skilled in the art and it is intended to cover such modifications as fall within the scope of the appended claims.

CLAIMS:

1. A blood vessel cross-sectional area detector comprising:

a catheter having at least a first pair of electrodes spaced apart from one another, and a second pair of electrodes spaced apart from one another;

means for measuring a voltage developed between said second pair of electrodes when a current is passed through said first pair of electrodes while inserted into a blood vessel;

means for converting said measured voltage into an impedance value representing a cross-sectional area of said blood vessel, and calculating said cross-sectional area;

means for measuring blood pressure in said blood vessel;

means for calculating a compliance value of said blood vessel based on said cross-sectional area and blood pressure; and

means for displaying said calculated blood vessel compliance value.

2. The detector of claim 1 wherein said first pair of electrodes is spaced apart with a predetermined, variable spacing within which said second pair of electrodes is disposed with a predetermined, variable spacing.

3. The detector of claim 1 wherein said voltage developed between said second pair of electrodes is

presented as a differential voltage to said measuring means which comprises an instrumentation amplifier, filters, an absolute value detector and A/D converter, for providing a proportional DC output voltage.

4. The detector of claim 1 wherein said means for measuring blood pressure comprises a pressure transducer disposed in said catheter between said second pair of electrodes.

5. The detector of claim 1 wherein said blood pressure and impedance values are measured continuously to provide dynamic values of said cross-sectional area and blood vessel compliance.

6. The detector of claim 5 wherein said dynamic blood vessel compliance value is measured at a point along said vessel.

7. A method of measuring blood vessel compliance using a blood vessel cross-sectional area detector comprising the steps of:

providing a catheter having at least a first pair of electrodes spaced apart from one another, and a second pair of electrodes spaced apart from one another;

measuring a voltage developed between said second pair of electrodes when a current is passed through said first pair of electrodes while inserted into a blood vessel;

converting said measured voltage into an impedance value representing a cross-sectional area of said blood

vessel, and calculating said cross-sectional area;

measuring blood pressure in said blood vessel;

calculating a compliance value of said blood vessel based on said cross-sectional area and blood pressure; and

displaying said calculated blood vessel compliance value.

8. The method of claim 7 wherein said first pair of electrodes is spaced apart with a predetermined, variable spacing within which said second pair of electrodes is disposed with a predetermined, variable spacing.

9. The method of claim 7 wherein said blood pressure and impedance values are measured continuously to provide dynamic values of said cross-sectional area and blood vessel compliance.

10. The method of claim 9 wherein said dynamic blood vessel compliance value is measured at a point along said vessel.

11. The method of claim 7 wherein said voltage measurement is made during a stenosis search procedure, said procedure comprising the steps of:

withdrawing said catheter away from an origin point in said blood vessel to several locations with respect thereto;

performing said impedance conversion to determine

said blood vessel cross-sectional area at each of said locations;

extracting a blood vessel diameter value from said cross-sectional area at each of said locations; and

comparing said diameter values at said locations to determine a blood vessel narrowing location comprising a stenosis.

12. The method of claim 7 performed in coronary arteries.

13. A blood vessel cross-sectional area detector substantially as described herein by way of example and with reference to the drawings.

14. A method of measuring blood vessel compliance using a blood vessel cross-sectional area detector, substantially as described herein by way of example and with reference to the drawings.

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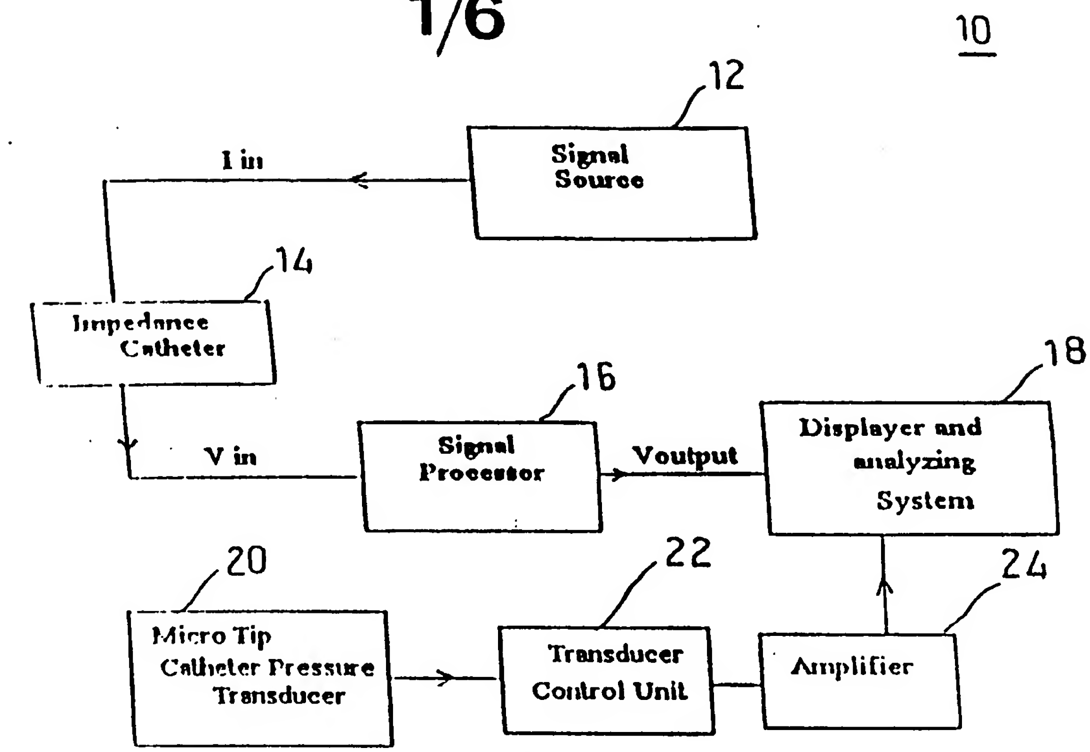
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Transducer Control Unit
Amplifier

Fig.1

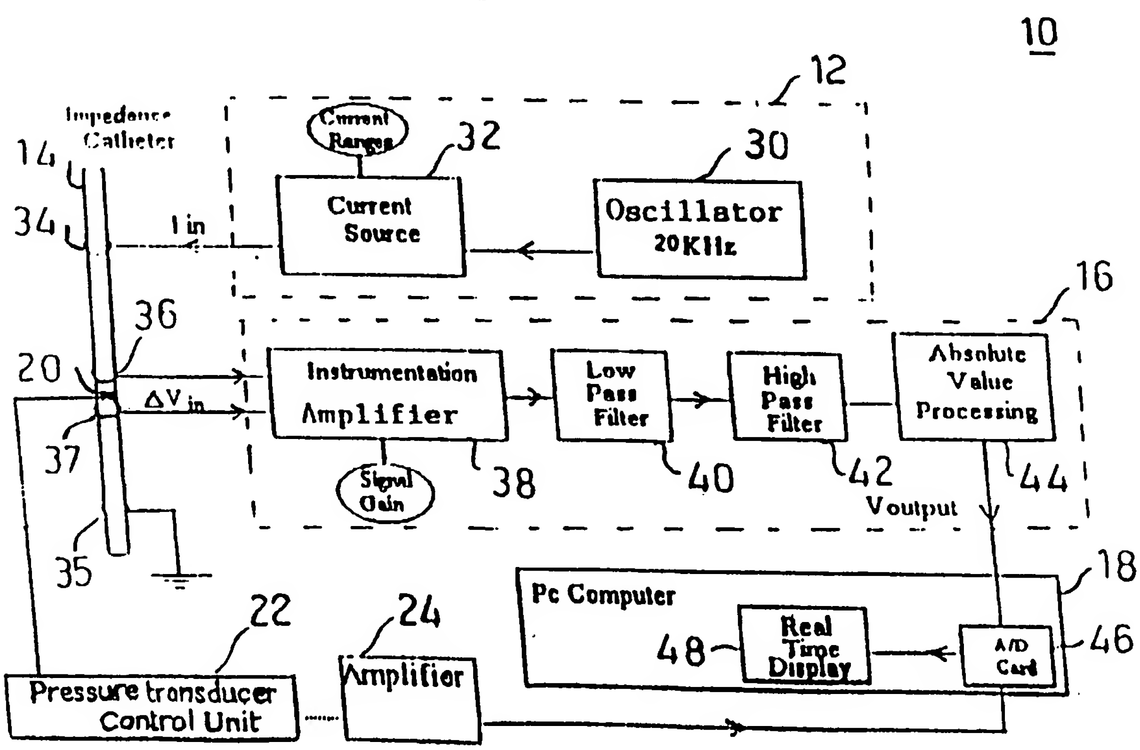
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Fig. 2

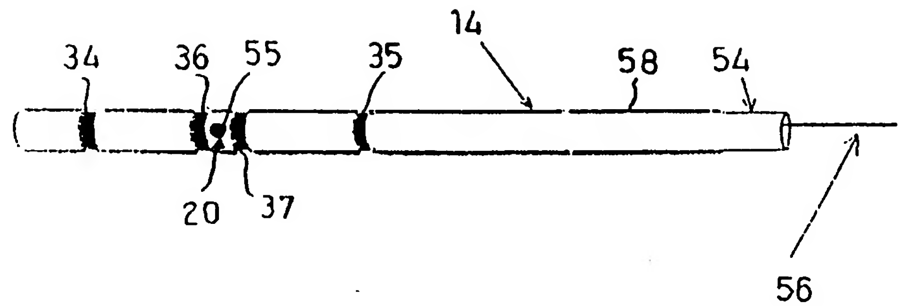
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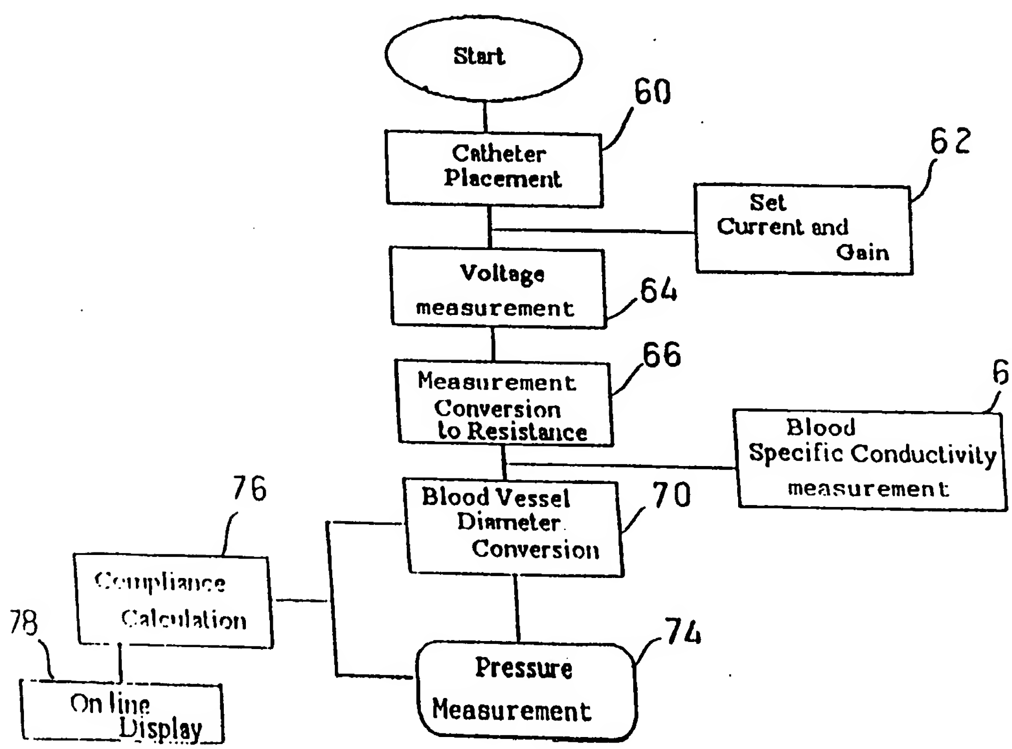
Fig. 3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Compliance Calculation
78
On line Display
Pressure Measurement
74

Fig. 4

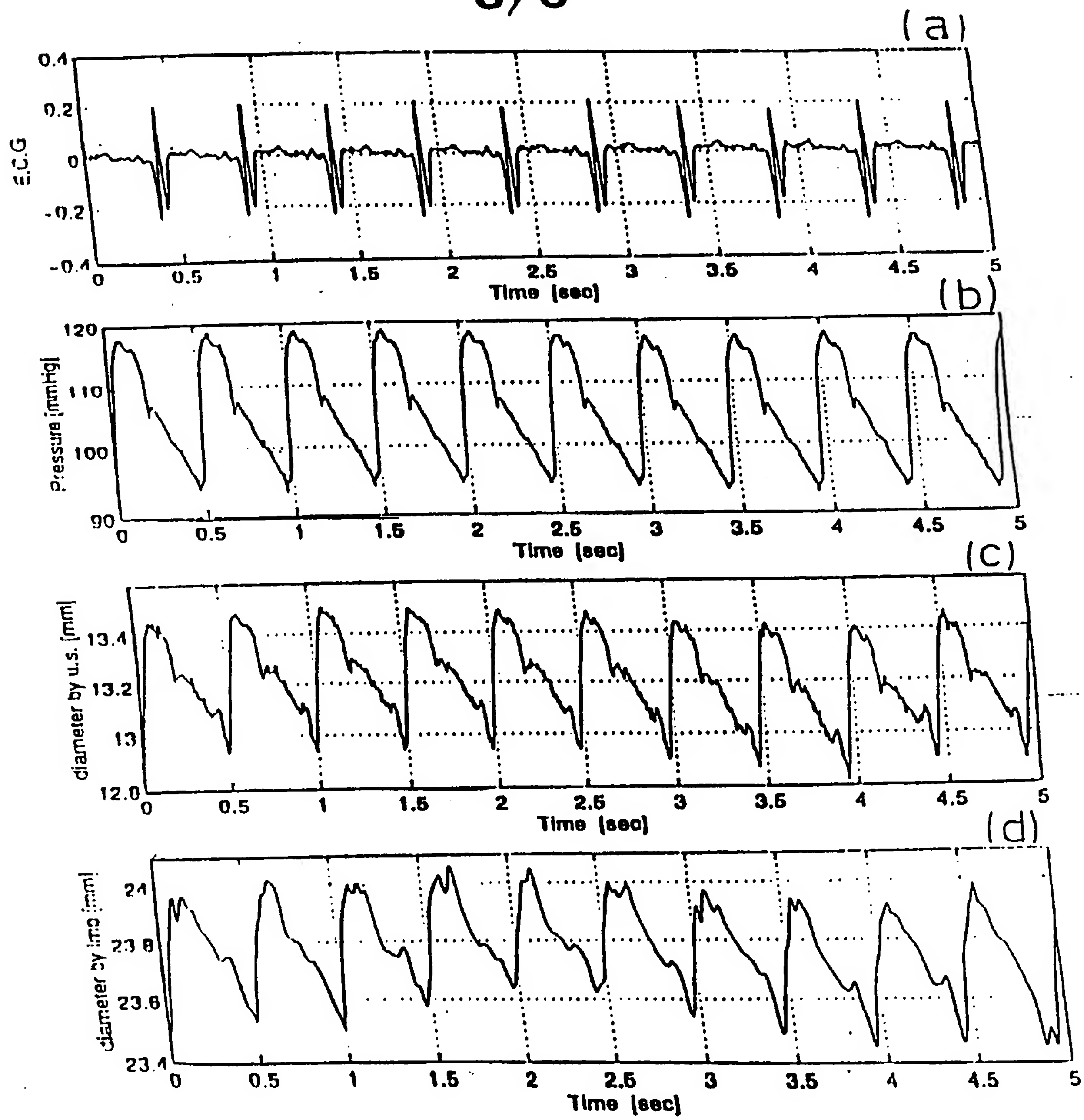
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Fig. 5

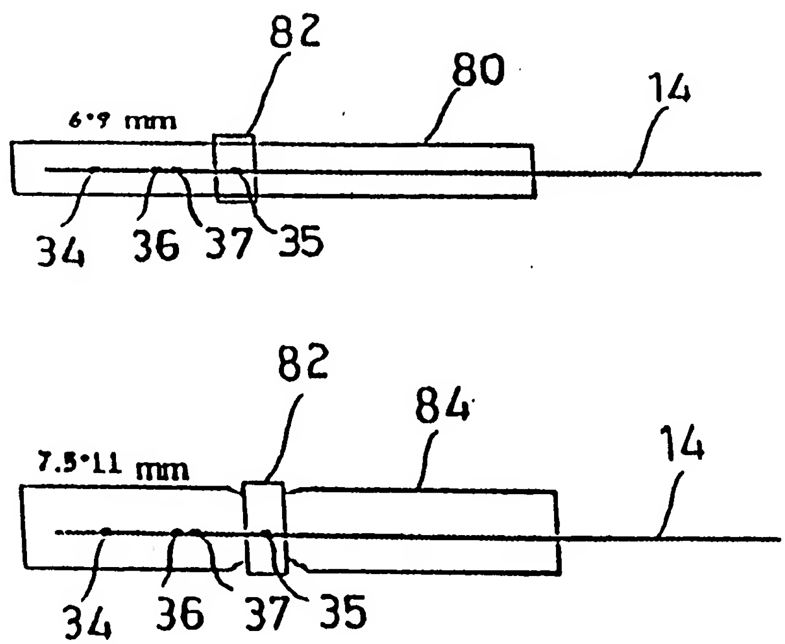
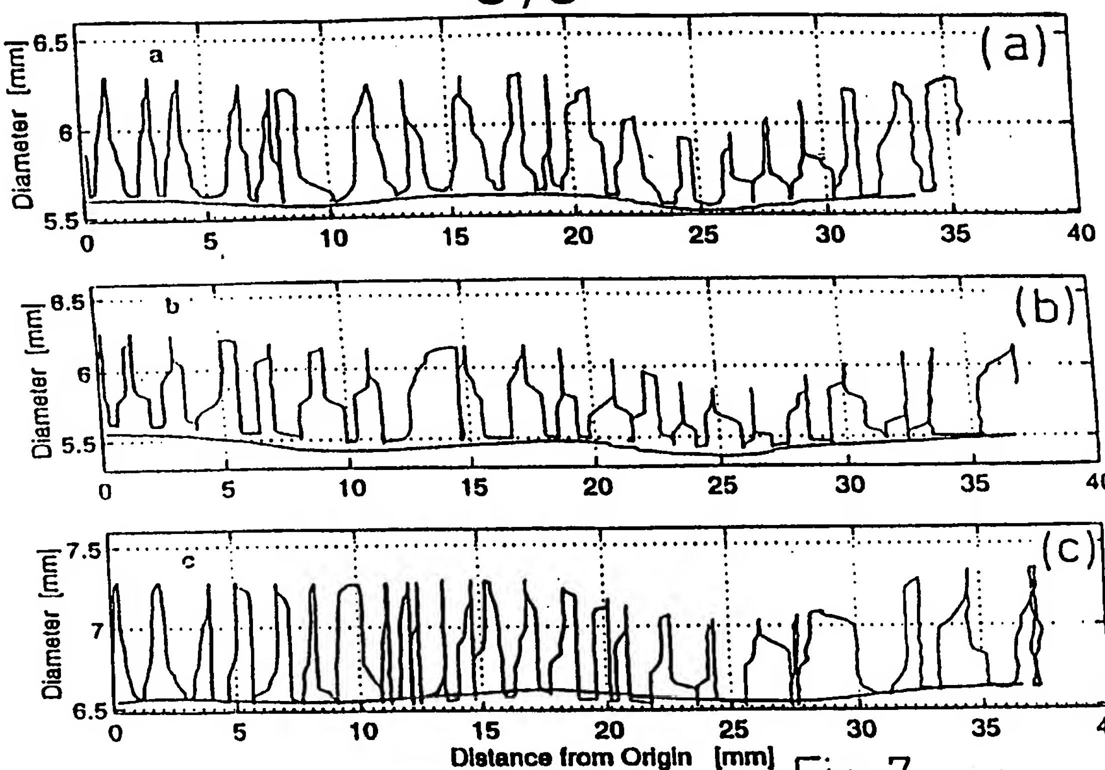


Fig.6



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(b)
b
(c)
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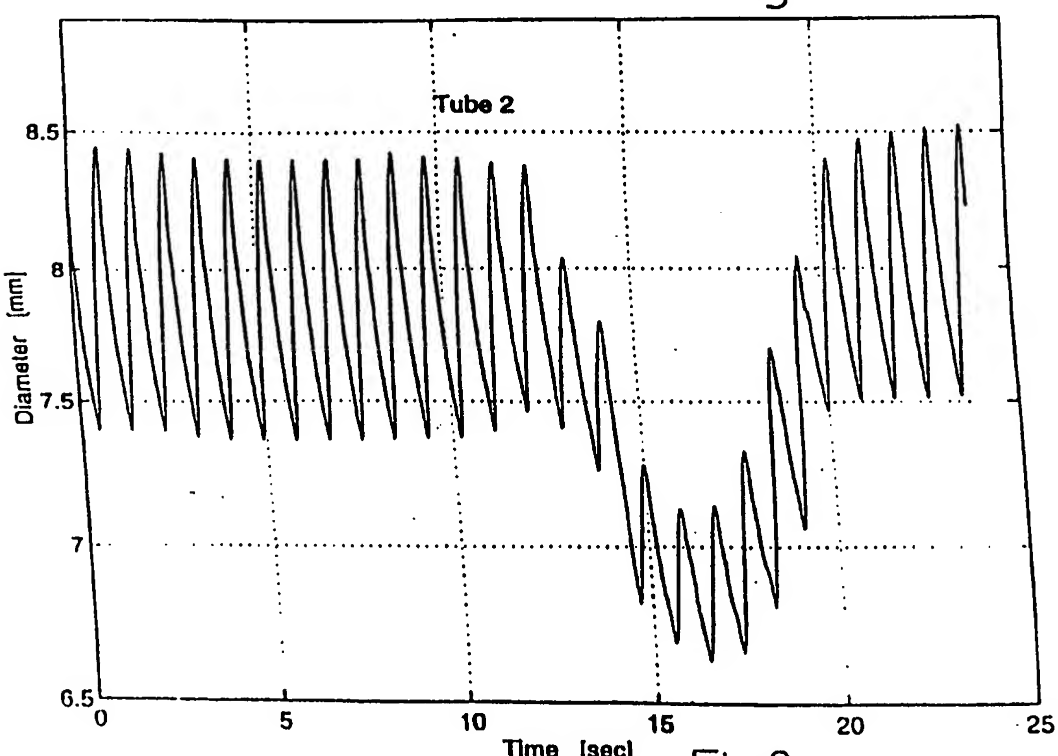
Fig. 7



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Time [sec]

Fig.8

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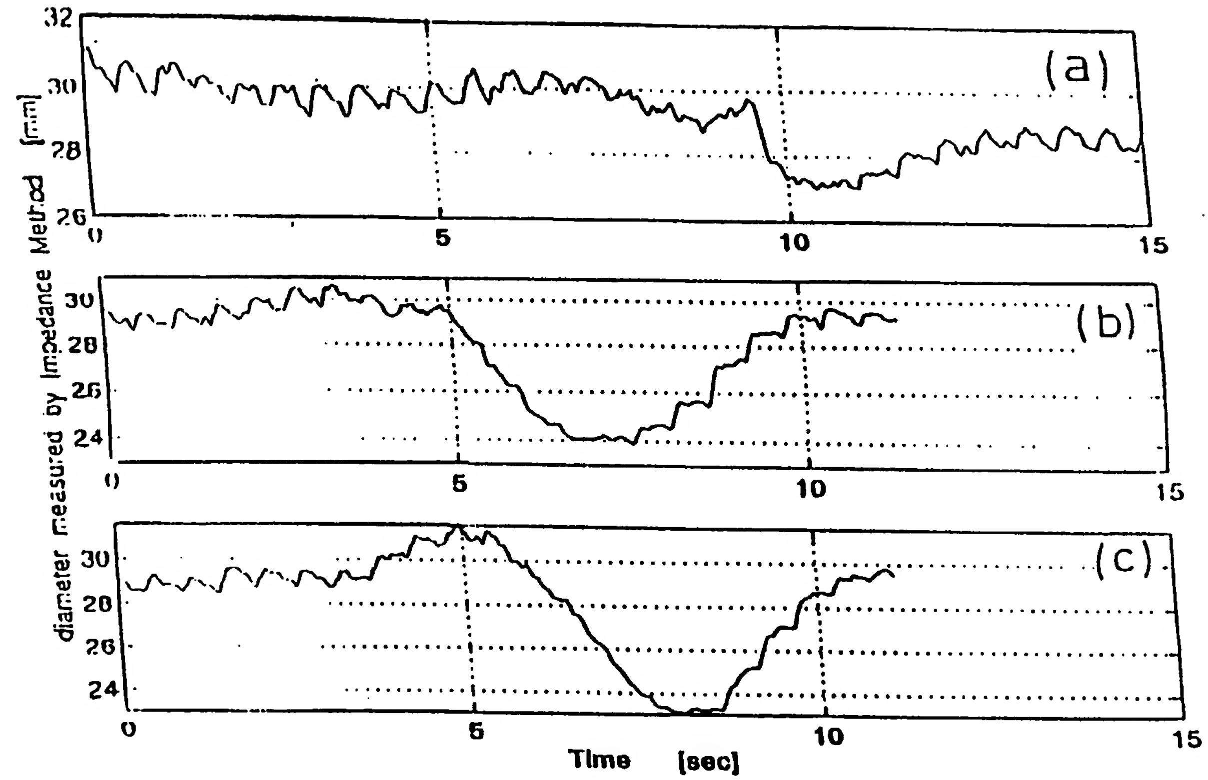

Fig.9

Table 1

	Search 1	search 2	Search 3
Diameter narrowing (mm)	3.08mm	5.3mm	7.02mm
Narrowing %	18.7%	32%	42.6%
Measured narrowing (mm)	2.74mm	4.7mm	5.5mm
Narrowing %	16.6%	28.6%	33.4%

Fig.10

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL98/00063

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61B 5/04
US CL :600/547
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 600/512, 547; 606/192, 374

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A, P	US 5,603,333 A (KONINGS) 18 FEBRUARY 1997, ENTIRE DCUMENT.	1-14
A	US 5,579,764 A (GOLDREYER) 03 DECEMBER 1996, ENTIRE DOCUMENT.	1-14
A, E	US 5,741,214 A (OUCHI ET AL) 21 APRIL 1998, ENTIRE DOCUMENT.	1-14
A	US 4,852,580 A (WOOD) 01 AUGUST 1989, ENTIRE DOCUMENT.	1-14

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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"&" document member of the same patent family

Date of the actual completion of the international search
07 JUNE 1998

Date of mailing of the international search report
08 JUL 1998

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